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Wang

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(54) **THROUGH FOCUS RETINAL IMAGE CAPTURING**

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CPC **A61B 3/12** (2013.01); **A61B 3/0008** (2013.01); **A61B 3/0025** (2013.01);

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(58) **Field of Classification Search**

CPC .. **A61B 3/12**; **A61B 3/14**; **A61B 3/135**; **A61B 3/117**; **A61B 3/1015**; **A61B 3/103**;

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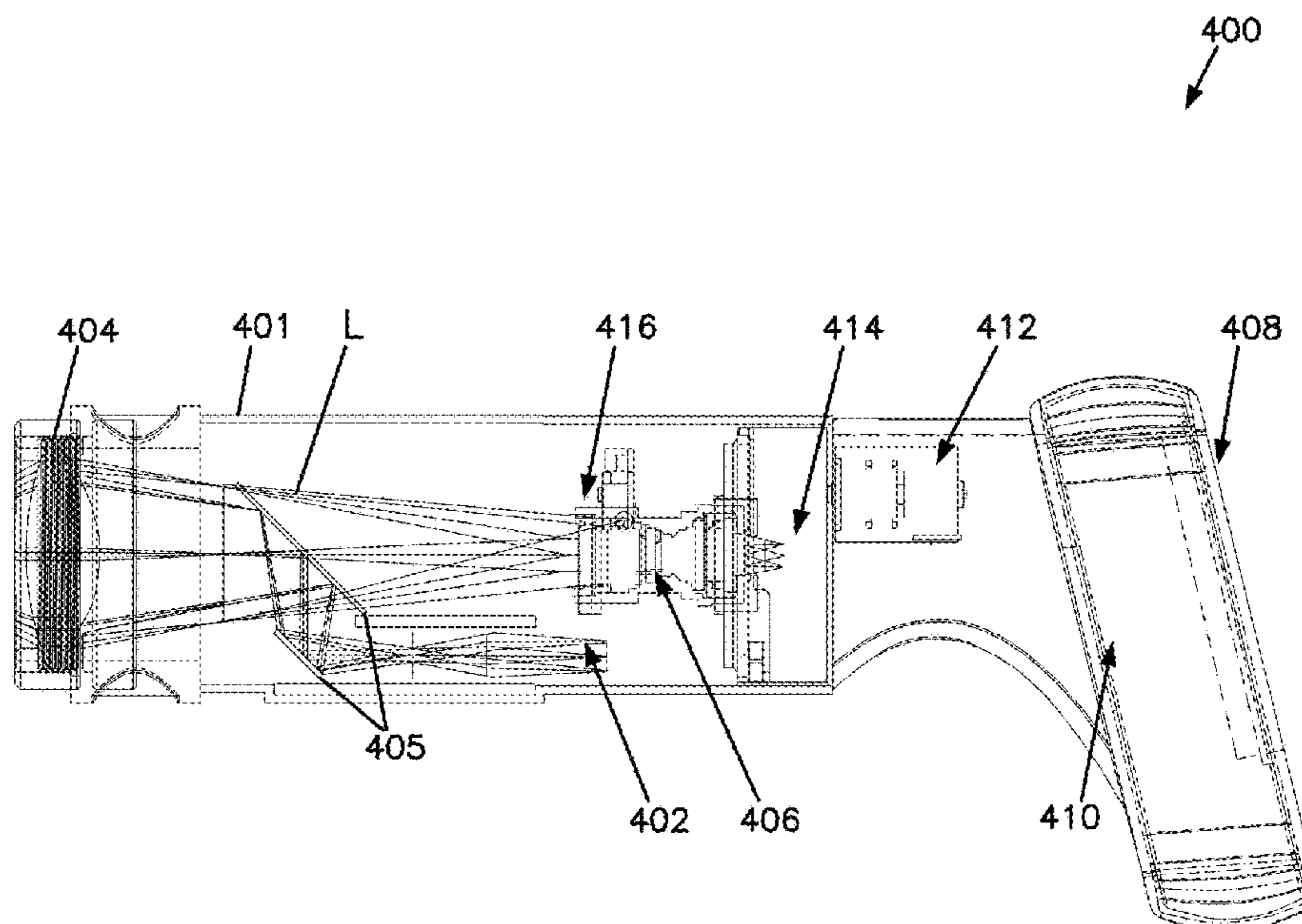
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(57) **ABSTRACT**

An apparatus for producing a non-mydratic fundus image is disclosed. The apparatus can include a processor and memory, as well as an illumination component and a camera with a variable focus lens. The apparatus can be configured to adjust the focus of the lens to a plurality of different diopter ranges and capture at least one image at each of the plurality of different diopter ranges. Using the captured images, three-dimensional maps of the fundus may be generated. Three-dimensional maps of the fundus may be used to screen or diagnose various diseases.

20 Claims, 12 Drawing Sheets



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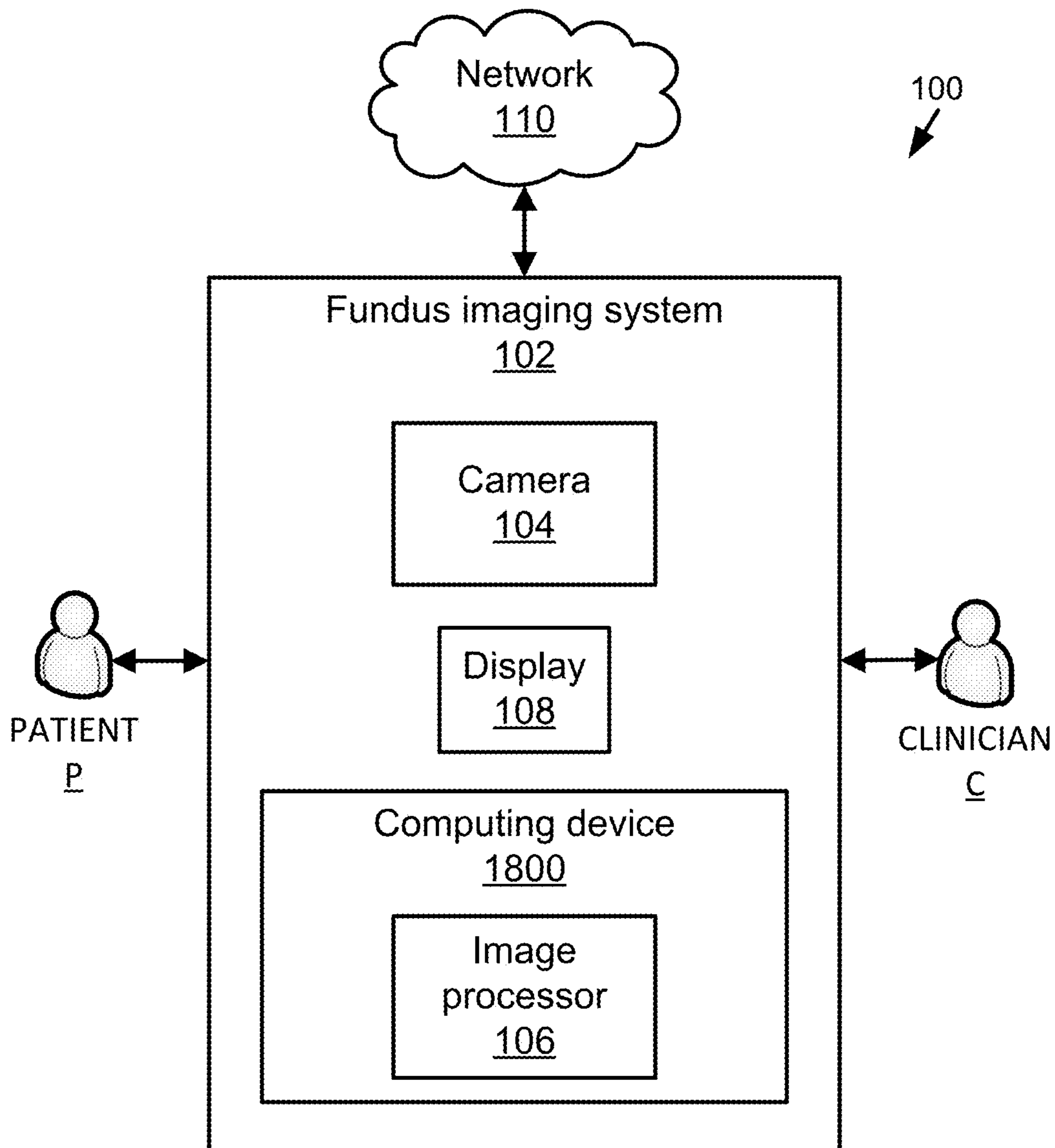


FIG. 1

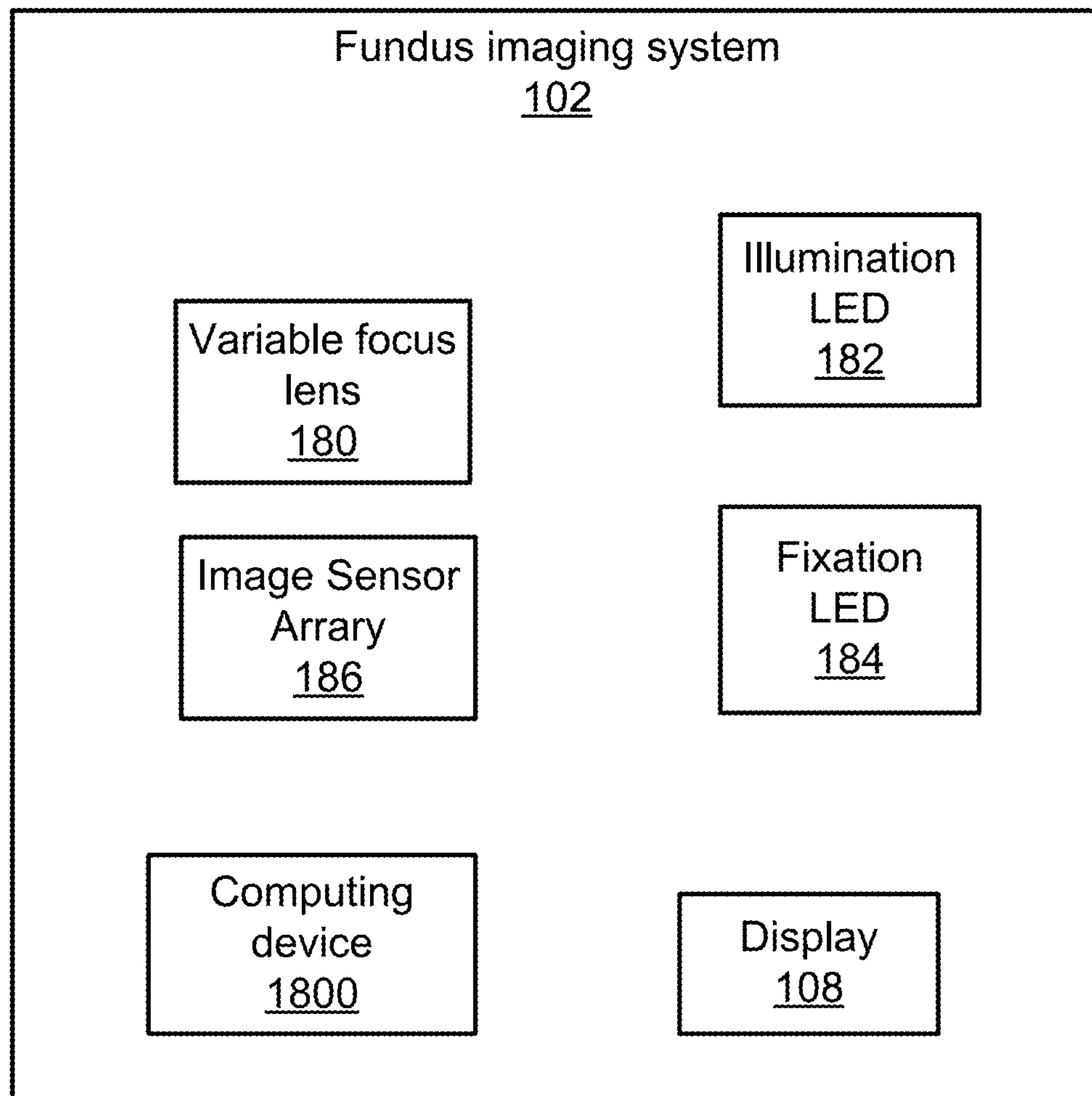


FIG. 2

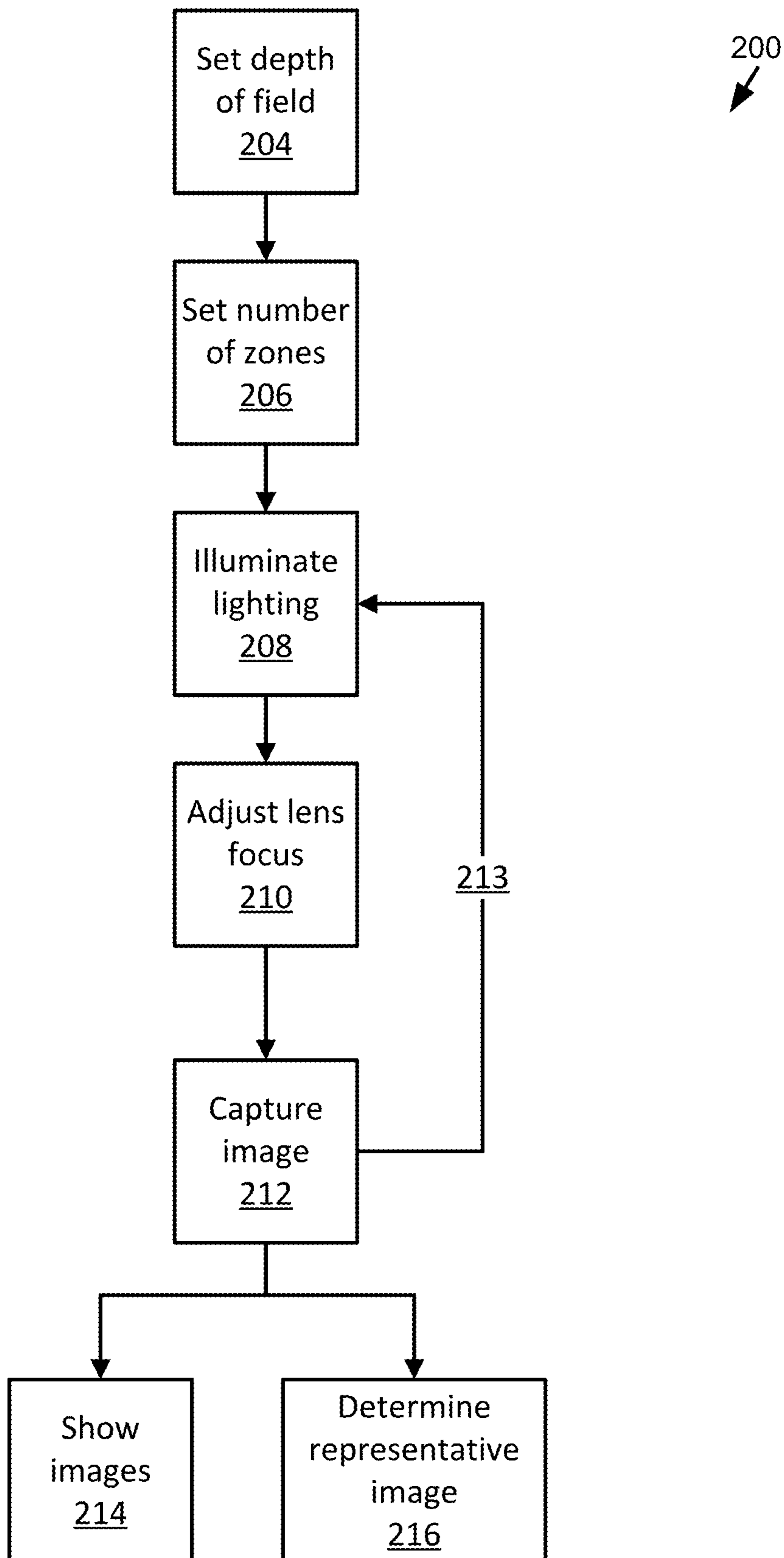


FIG. 3

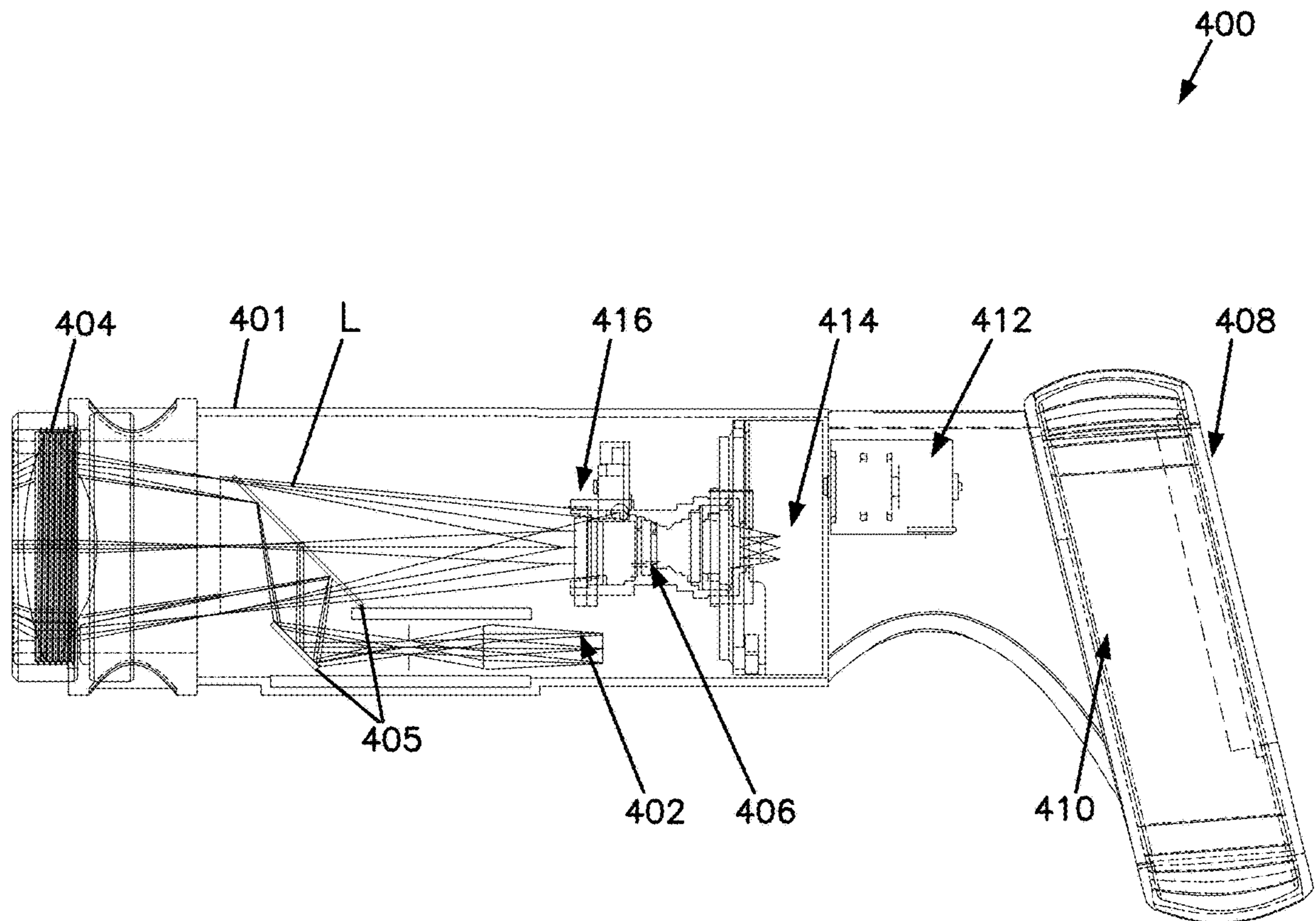


FIG. 4

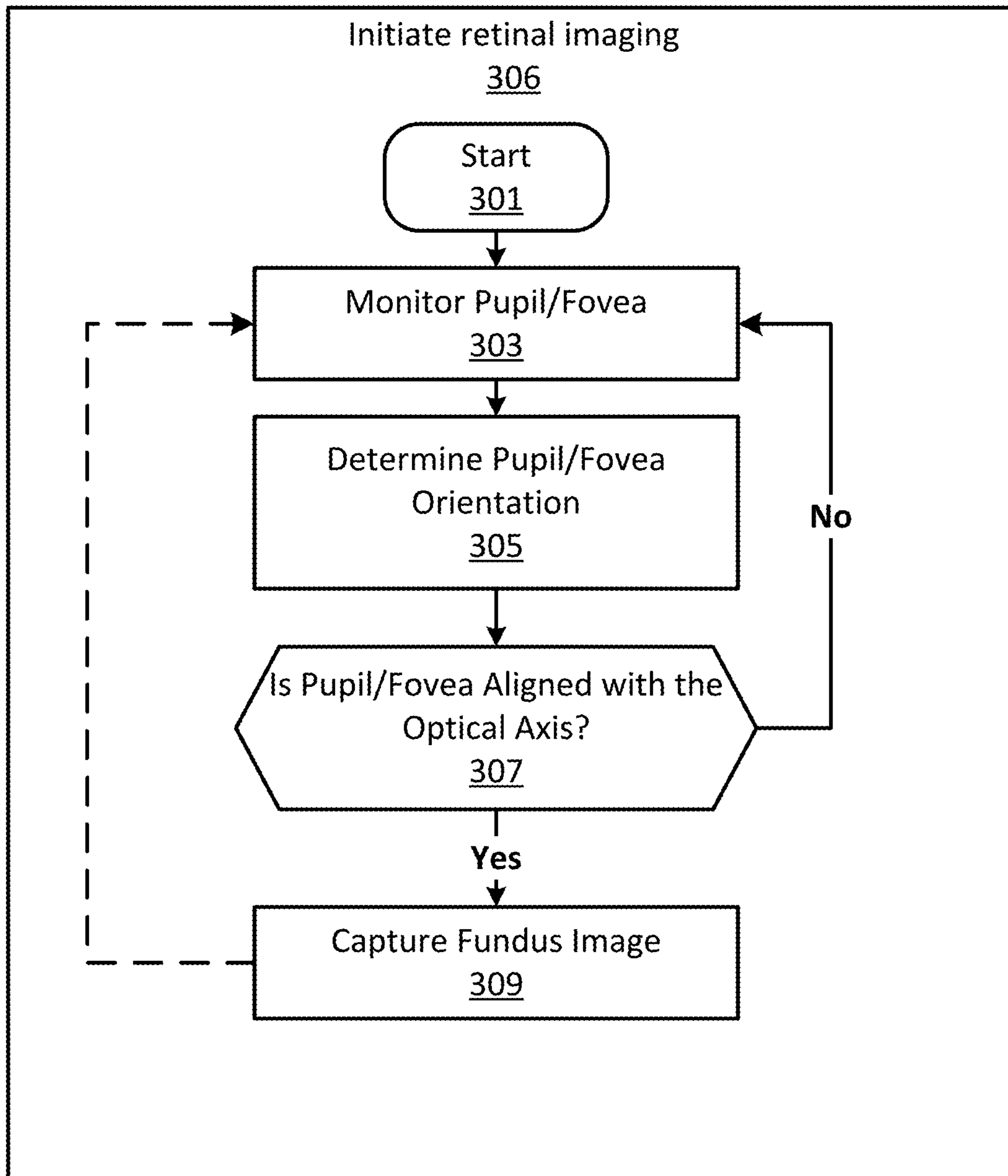


FIG. 5

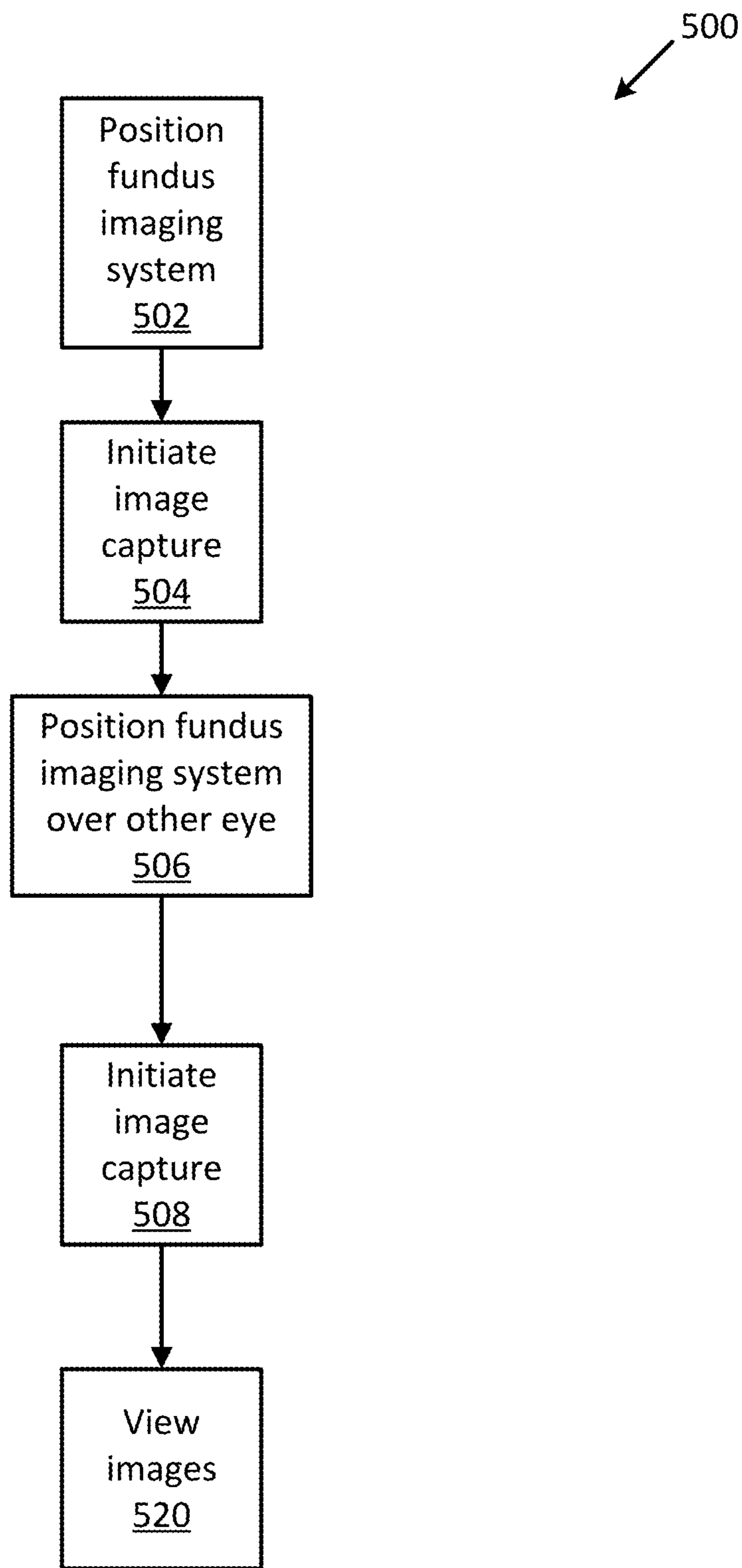


FIG. 6

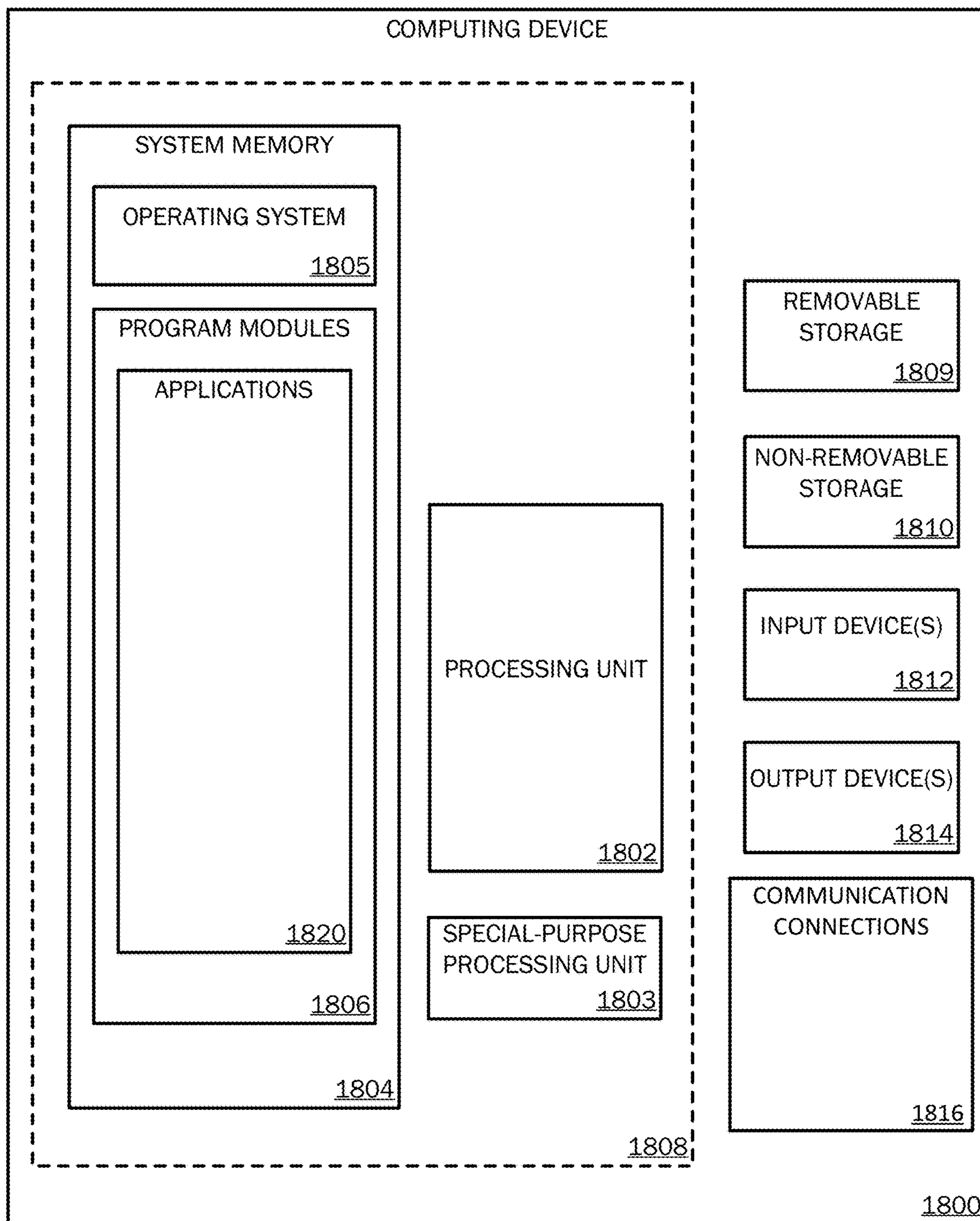
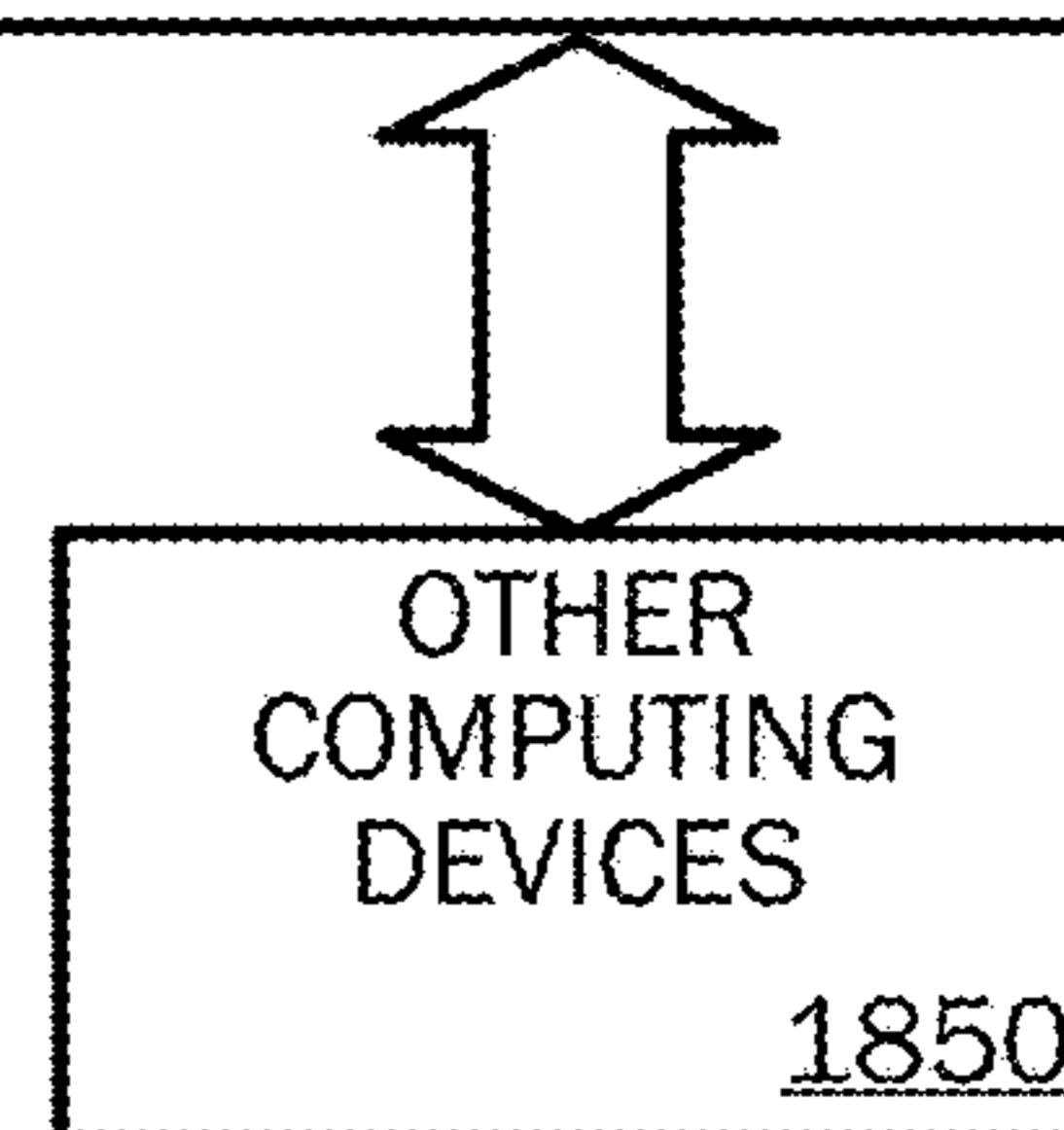


FIG. 7



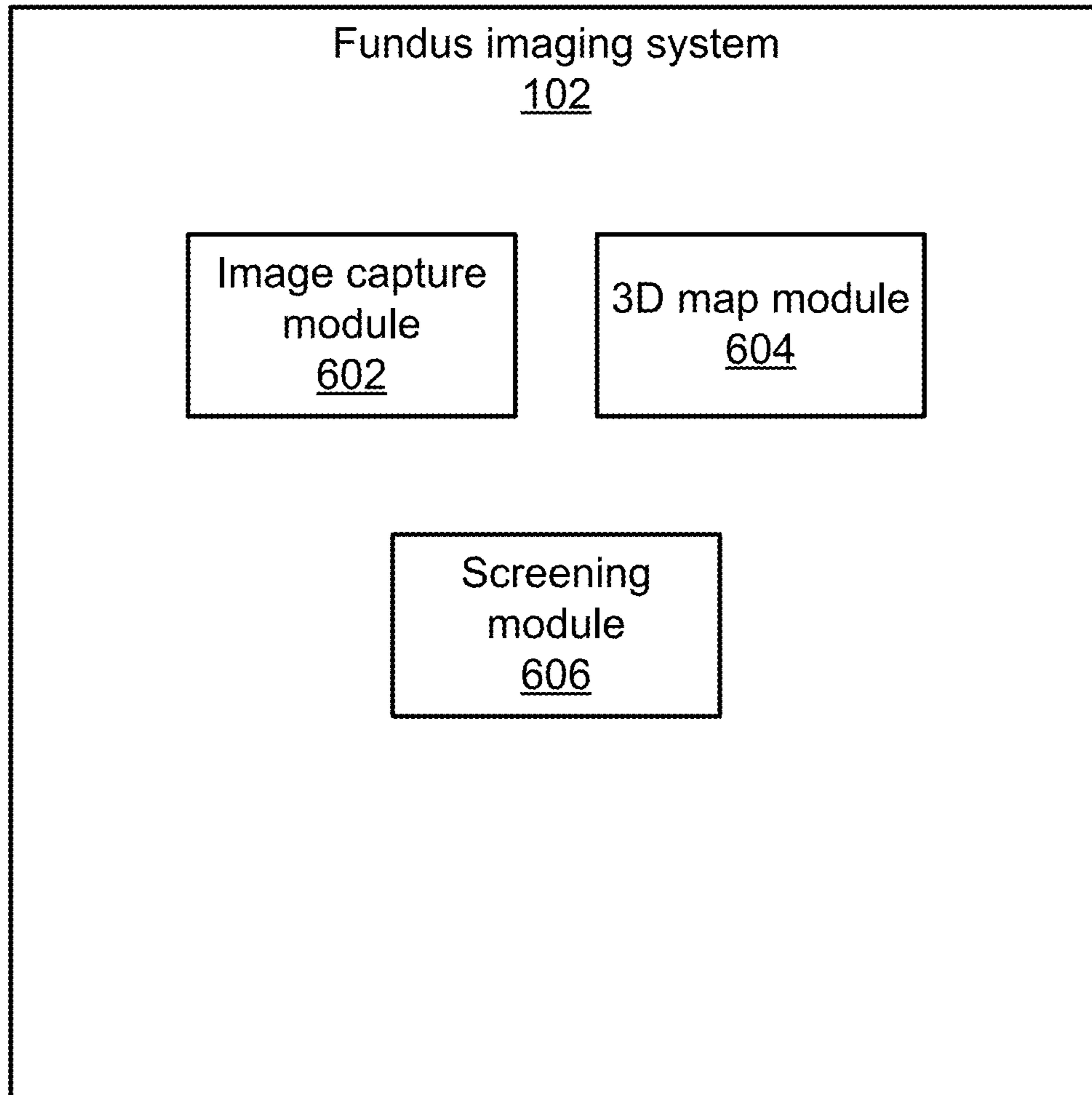


FIG. 8

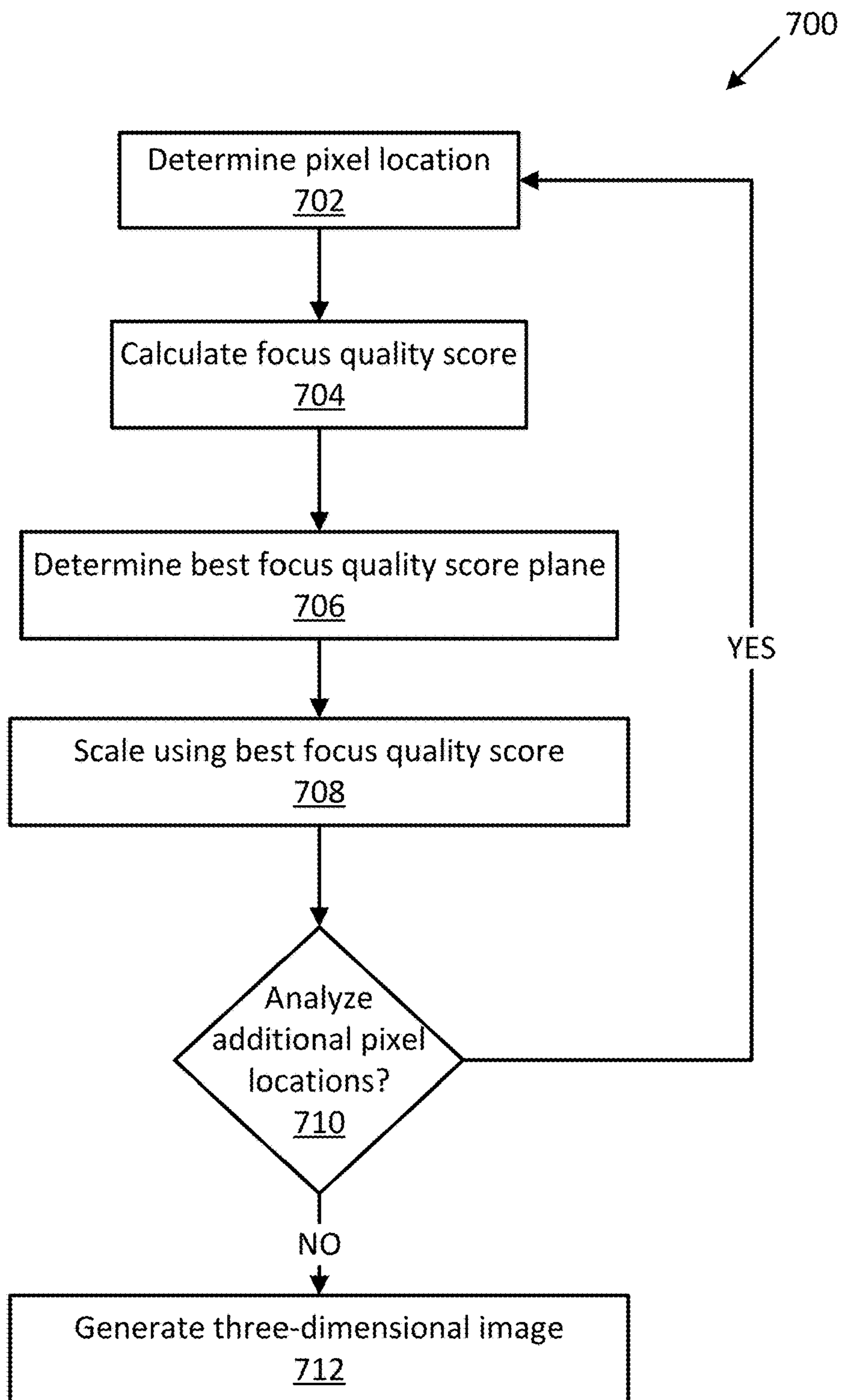


FIG. 9

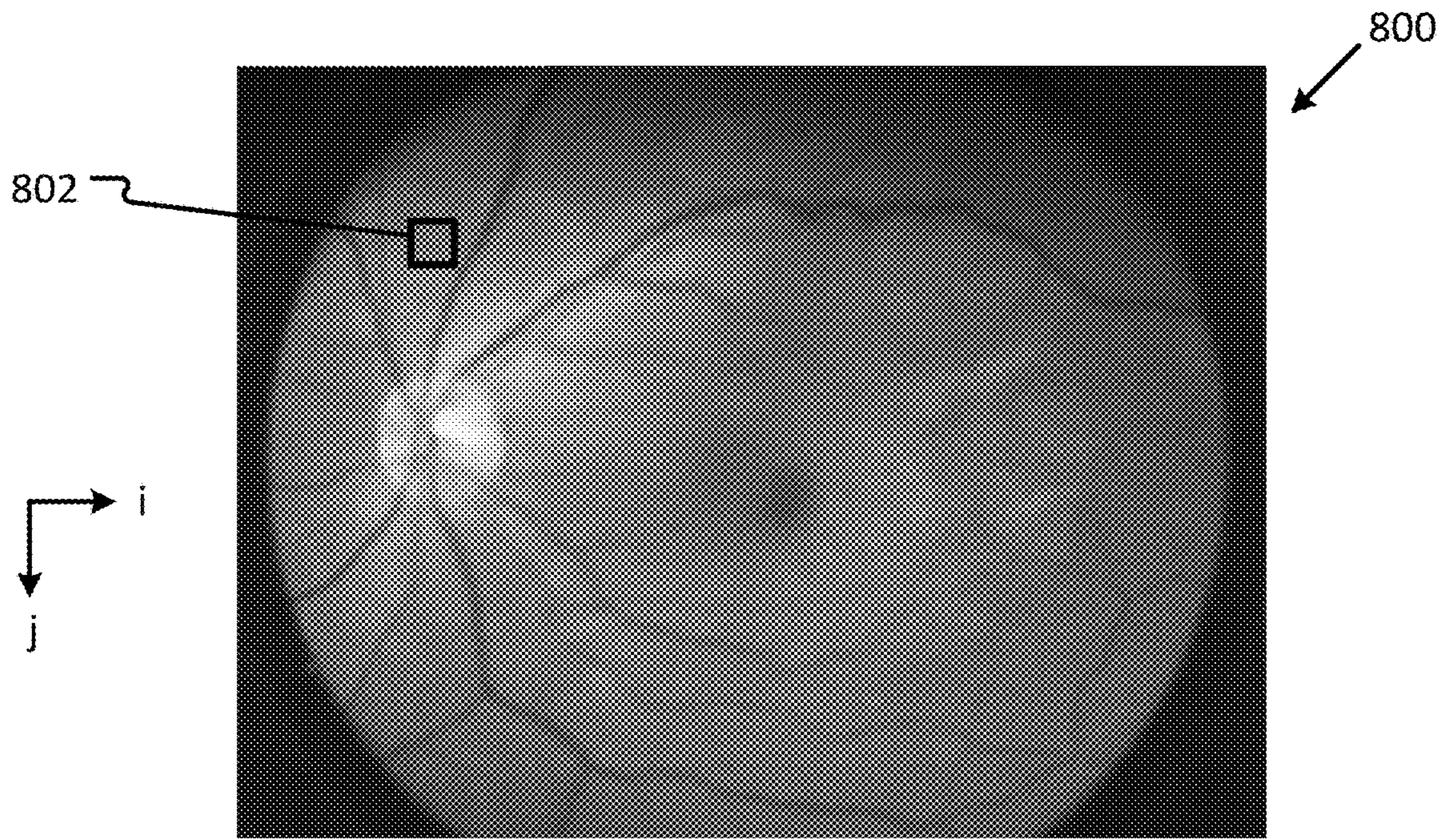


FIG. 10A

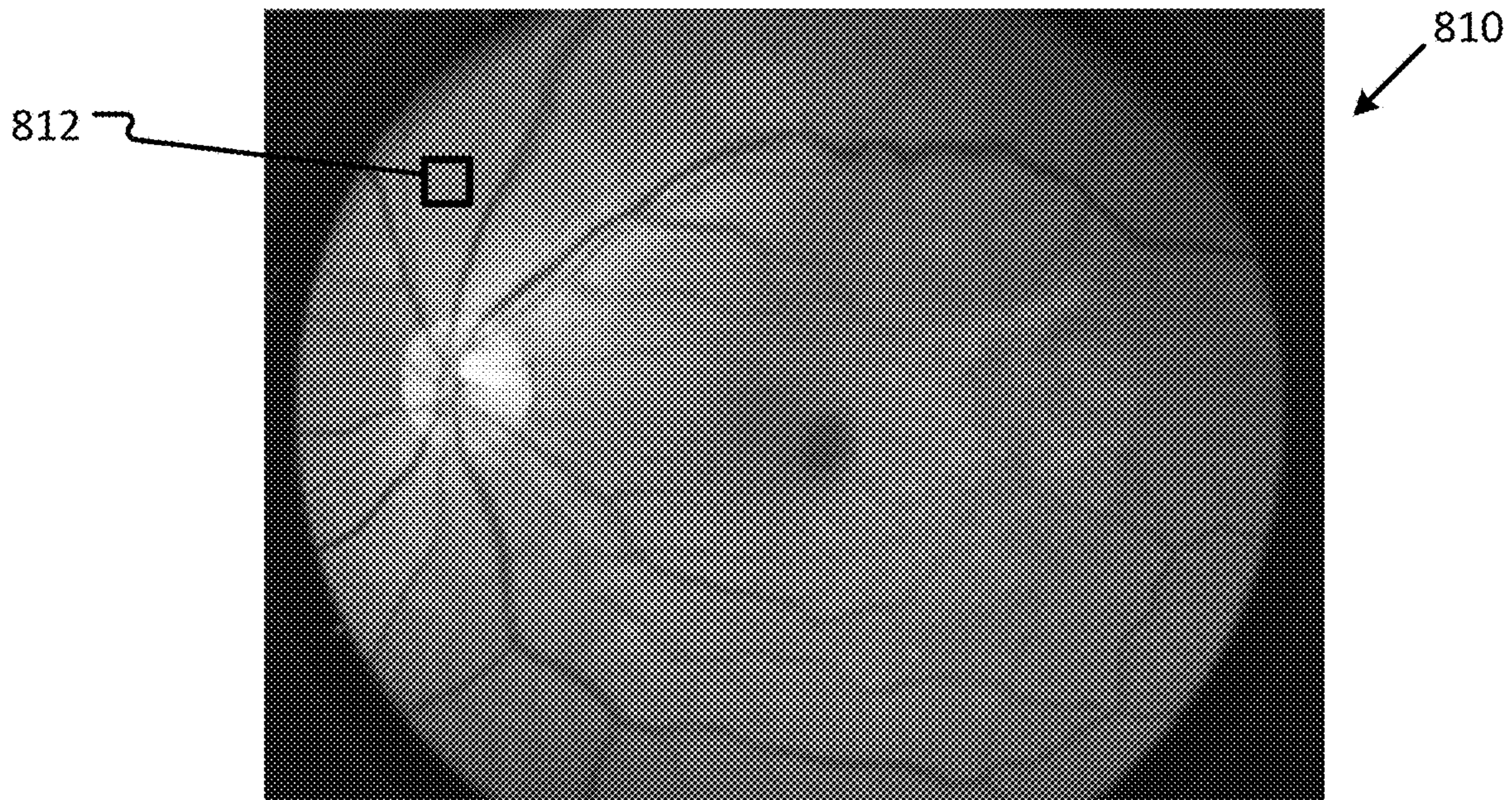


FIG. 10B

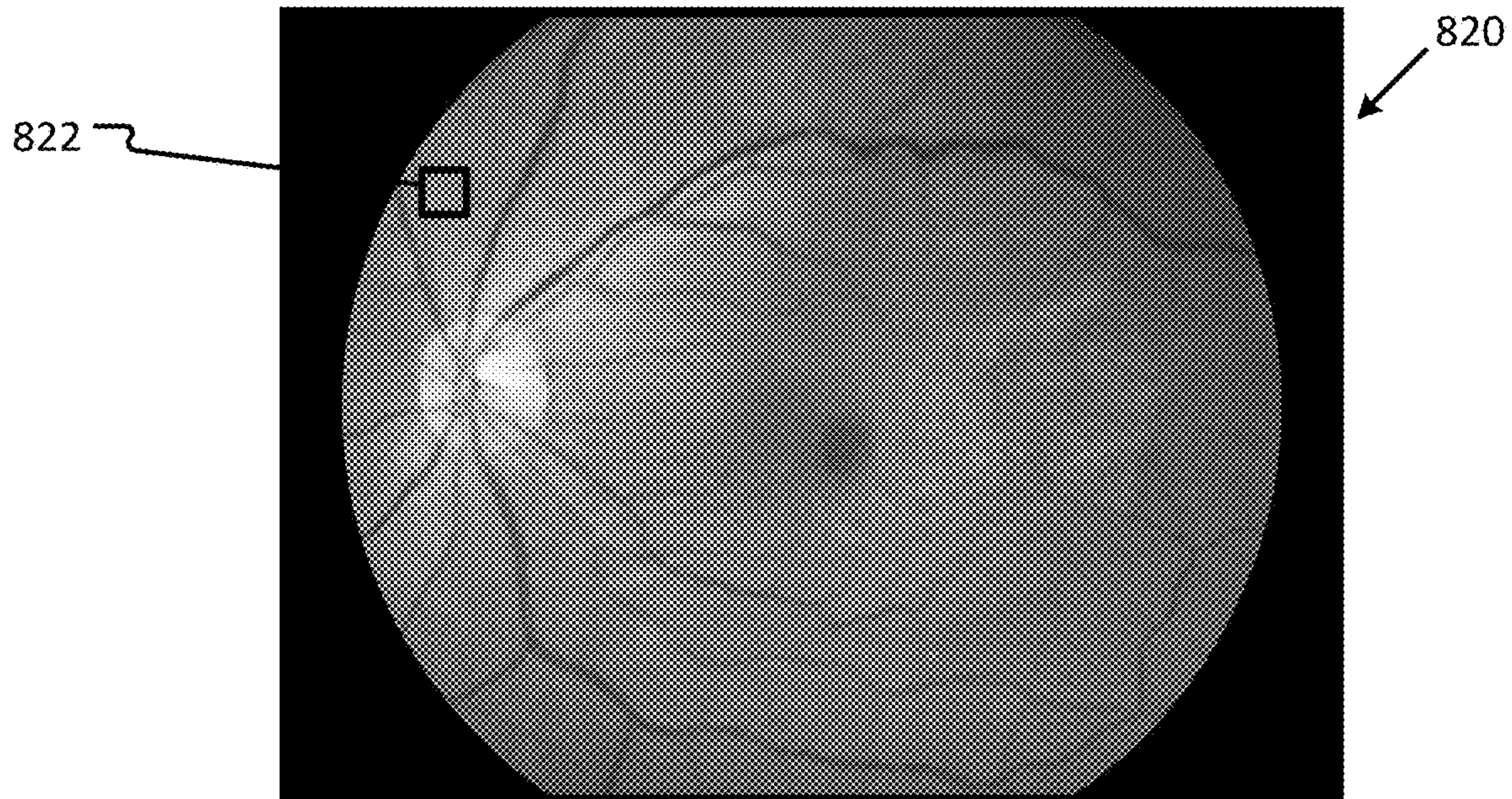


FIG. 10C

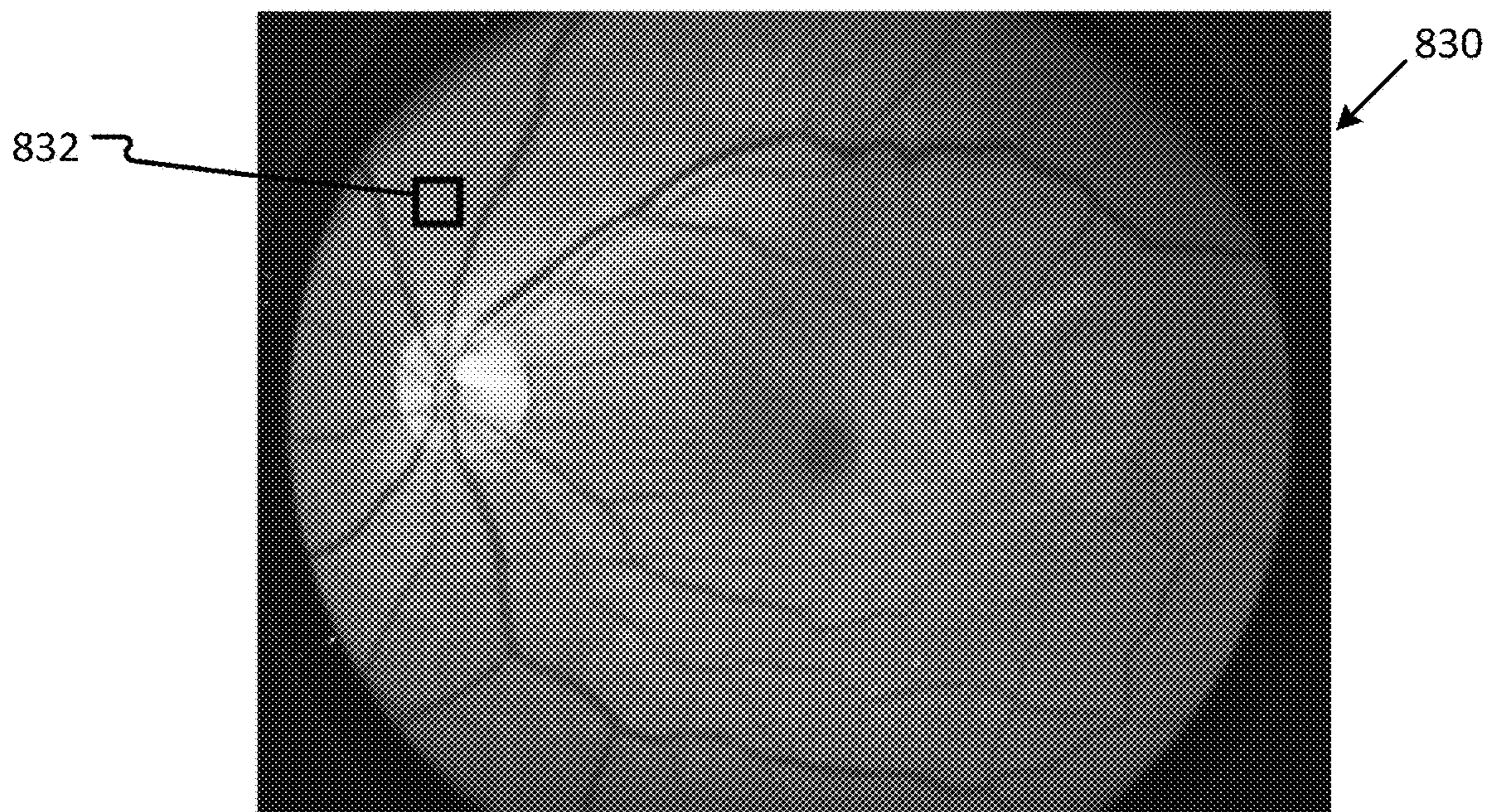


FIG. 10D



FIG. 10E

1

THROUGH FOCUS RETINAL IMAGE CAPTURING

INTRODUCTION

People with type 1 or type 2 diabetes can develop eye disease as a result of having diabetes. One of the most common diabetic eye diseases is diabetic retinopathy, which is damage to the blood vessels of the light-sensitive tissue at the back of the eye, known as the retina. Trained medical professionals use cameras during eye examinations for diabetic retinopathy screening. The cameras can produce images of the back of the eye and trained medical professionals use those images to diagnose and treat diabetic retinopathy.

These images are produced either with pharmacological pupil dilation, known as mydriatic fundus imaging, or without pharmacological pupil dilation, known as non-mydriatic fundus imaging. Because pupil dilation is inversely related, in part, to the amount of ambient light, non-mydriatic fundus imaging usually occurs in low lighting environments. Medical professionals can also use fundus imaging apparatus to detect or monitor other diseases, such as hypertension, glaucoma, and papilledema.

SUMMARY

In one aspect a non-mydriatic fundus imaging apparatus is disclosed. The apparatus includes a processor and memory and a camera including a lens, where the camera is operatively coupled to the processor. The memory may store instructions that, when executed by the processor, cause the apparatus to: adjust a focus of the lens to a plurality of different diopter ranges, capture a plurality of images of a fundus, wherein the camera captures at least one image at each of the plurality of different diopter ranges; and, after capturing each of the plurality of images of the fundus, generate a three-dimensional map of the fundus.

In another aspect, a method for screening for optic nerve edema with a non-mydriatic fundus imaging apparatus is disclosed. The method includes adjusting a lens of a camera to focus on each of a plurality of zones in a depth of field, capturing at least one image at each of the plurality of zones, generating a three-dimensional map of a fundus using the at least one image captured at each of the plurality of zones, and, based on the three-dimensional map, screening for optic nerve edema.

In another aspect, a non-mydriatic fundus image capture system is disclosed. The system includes a housing, an image capture device coupled to the housing, a display, a processing unit, and memory. The memory may store instructions that, when executed by the processing unit, cause the system to: capture a plurality of images of a fundus in an image capture mode, where the image capture mode includes a plurality of adjustments of a lens of the image capture device such that the image capture device captures an image at each of the plurality of adjustments in a depth of field focus range; after capturing each of the plurality of images of the fundus, generate a three-dimensional map of the fundus, including identifying a first region, each of the plurality of images having corresponding first regions; and applying a focus metric on each of the respective first regions of each of the plurality of images, thereby generating a focus metric score for each of the respective first regions of each of the plurality of images; identify one or more areas

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of interest on the three-dimensional map of the fundus; and screen the one or more areas of interest for indications of disease.

DESCRIPTION OF THE FIGURES

The following figures, which form a part of this application, are illustrative of described technology and are not meant to limit the scope of the claims in any manner, which scope shall be based on the claims appended hereto.

FIG. 1 is an embodiment of an example system for recording and viewing an image of a patient's fundus;

FIG. 2 is an embodiment of an example fundus imaging system;

FIG. 3 is an embodiment of an example method for imaging a patient's fundus using a fundus imaging system;

FIG. 4 is an embodiment of an example fundus imaging system;

FIG. 5 illustrates an example method of initiating a fundus imaging using passive eye tracking;

FIG. 6 is an embodiment of an example use of a fundus imaging system; and

FIG. 7 is an example computing device used within the fundus imaging system.

FIG. 8 illustrates logical components of another embodiment of the fundus imaging system.

FIG. 9 is an embodiment of an example method for processing a set of images captured by a fundus imaging system.

FIG. 10A is an example image captured with an embodiment of the fundus imaging system at a first focus.

FIG. 10B is an example image captured with an embodiment of the fundus imaging system at a second focus.

FIG. 10C is an example image captured with an embodiment of the fundus imaging system at a third focus.

FIG. 10D is an example image captured with an embodiment of the fundus imaging system at a fourth focus.

FIG. 10E is an example image captured with an embodiment of the fundus imaging system at a fifth focus.

DETAILED DESCRIPTION

FIG. 1 is a schematic block diagram illustrating an example system **100** for recording and viewing an image of a patient's fundus. In this example, the system **100** includes a patient **P**, a fundus imaging system **102**, a computing device **1800** including an image processor **106**, a camera **104** in communication with the computing device **1800**, a display **108** in communication with the computing device **1800** and used by clinician **C**, and a network **110**. An embodiment of the example fundus imaging system **102** is shown and described in more detail below with reference to FIG. 4.

The fundus imaging system **102** functions to create a set of digital image of a patient's **P** eye fundus. As used herein, "fundus" refers to the eye fundus and includes the retina, optic nerve, macula, vitreous, choroid and posterior pole.

In this example, one or more images of the eye are desired. For instance, the patient **P** is being screened for an eye disease, such as diabetic retinopathy. The fundus imaging system **102** can also be used to provide images of the eye for other purposes, such as to diagnose or monitor the progression of a disease such as diabetic retinopathy.

The fundus imaging system **102** includes a handheld housing that supports the system's components. The housing supports one or two apertures for imaging one or two eyes at a time. In embodiments, the housing supports positional guides for the patient **P**, such as an optional adjustable chin

rest. The positional guide or guides help to align the patient's P eye or eyes with the one or two apertures. In embodiments, the housing supports means for raising and lowering the one or more apertures to align them with the patient's P eye or eyes. Once the patient's P eyes are aligned, the clinician C then initiates the image captures by the fundus imaging system **102**.

One technique for fundus imaging requires mydriasis, or the dilation of the patient's pupil, which can be painful and/or inconvenient to the patient P. Example system **100** does not require a mydriatic drug to be administered to the patient P before imaging, although the system **100** can image the fundus if a mydriatic drug has been administered.

The system **100** can be used to assist the clinician C in screening for, monitoring, or diagnosing various eye diseases, such as hypertension, diabetic retinopathy, glaucoma and papilledema. It will be appreciated that the clinician C that operates the fundus imaging system **102** can be different from the clinician C evaluating the resulting image.

In the example embodiment **100**, the fundus imaging system **102** includes a camera **104** in communication with an image processor **106**. In this embodiment, the camera **104** is a digital camera including a lens, an aperture, and a sensor array. The camera **104** lens is a variable focus lens, such as a lens moved by a step motor, or a fluid lens, also known as a liquid lens in the art. The camera **104** is configured to record images of the fundus one eye at a time. In other embodiments, the camera **104** is configured to record an image of both eyes substantially simultaneously. In those

embodiments, the fundus imaging system **102** can include two separate cameras, one for each eye.

In example system **100**, the image processor **106** is operatively coupled to the camera **104** and configured to communicate with the network **110** and display **108**.

The image processor **106** regulates the operation of the camera **104**. Components of an example computing device, including an image processor, are shown in more detail in FIG. 7, which is described further below.

The display **108** is in communication with the image processor **106**. In the example embodiment, the housing supports the display **108**. In other embodiments, the display connects to the image processor, such as a smart phone, tablet computer, or external monitor. The display **108** functions to reproduce the images produced by the fundus imaging system **102** in a size and format readable by the clinician C. For example, the display **108** can be a liquid crystal display (LCD) and active matrix organic light emitting diode (AMOLED) display. The display can be touch sensitive.

The example fundus imaging system **102** is connected to a network **110**. The network **110** may include any type of wireless network, a wired network, or any communication network known in the art. For example, wireless connections can include cellular network connections and connections made using protocols such as 802.11a, b, and/or g. In other examples, a wireless connection can be accomplished directly between the fundus imaging system **102** and an external display using one or more wired or wireless protocols, such as Bluetooth, Wi-Fi Direct, radio-frequency identification (RFID), or Zigbee. Other configurations are possible.

FIG. 2 illustrates components of an example fundus imaging system **102**. The example fundus imaging system **102** includes a variable focus lens **180**, an illumination LED **182**, an image sensor array **186**, a fixation LED **184**, a computing device **1800**, and a display **108**. Each component

is in electrical communication with, at least, the computing device **1800**. Other embodiments can include more or fewer components.

In one of the embodiments, the variable focus lens **180** is a liquid lens. A liquid lens is an optical lens whose focal length can be controlled by the application of an external force, such as a voltage. The lens includes a transparent fluid, such as water or water and oil, sealed within a cell and a transparent membrane. By applying a force to the fluid, the curvature of the fluid changes, thereby changing the focal length. This effect is known as electrowetting.

Generally, a liquid lens can focus between about -10 diopters to about $+30$ diopters. The focus of a liquid lens can be made quickly, even with large changes in focus. For instance, some liquid lenses can autofocus in tens of milliseconds or faster. Liquid lenses can focus from about 10 cm to infinity and can have an effective focal length of about 16 mm or shorter.

In another embodiment of example fundus imaging system **102**, the variable focus lens **180** is one or more movable lenses that are controlled by a stepping motor, a voice coil, an ultrasonic motor, or a piezoelectric actuator. Additionally, a stepping motor can also move the image sensor array **186**. In those embodiments, the variable focus lens **180** and/or the image sensor array **186** are oriented normal to an optical axis of the fundus imaging system **102** and move along the optical axis. An example stepping motor is shown and described below with reference to FIG. 4.

The example fundus imaging system **102** also includes an illumination light-emitting diode (LED) **182**. The illumination LED **182** can be single color or multi-color. For example, the illumination LED **182** can be a three-channel RGB LED, where each die is capable of independent and tandem operation.

Optionally, the illumination LED **182** is an assembly including one or more visible light LEDs and a near-infrared LED. The optional near-infrared LED can be used in a preview mode, for example, for the clinician C to determine or estimate the patient's P eye focus without illuminating visible light that could cause the pupil to contract or irritate the patient P.

The illumination LED **182** is in electrical communication with the computing device **1800**. Thus, the illumination of illumination LED **182** is coordinated with the adjustment of the variable focus lens **180** and image capture. The illumination LED **182** can be overdriven to draw more than the maximum standard current draw rating. In other embodiments, the illumination LED **182** can also include a near-infrared LED. The near-infrared LED is illuminated during a preview mode.

The example fundus imaging system **102** also optionally includes a fixation LED **184**. The fixation LED **184** is in communication with the computing device **1800** and produces a light to guide the patient's P eye for alignment. The fixation LED **184** can be a single color or multicolor LED. For example, the fixation LED **184** can produce a beam of green light that appears as a green dot when the patient P looks into the fundus imaging system **102**. Other colors and designs, such as a cross, "x" and circle are possible.

The example fundus imaging system **102** also includes an image sensor array **186** that receives and processes light reflected by the patient's fundus. The image sensor array **186** is, for example, a complementary metal-oxide semiconductor (CMOS) sensor array, also known as an active pixel sensor (APS), or a charge coupled device (CCD) sensor.

The image sensor array **186** has a plurality of rows of pixels and a plurality of columns of pixels. In some embodi-

ments, the image sensor array has about 1280 by 1024 pixels, about 640 by 480 pixels, about 1500 by 1152 pixels, about 2048 by 1536 pixels, or about 2560 by 1920 pixels.

In some embodiments, the pixel size in the image sensor array **186** is from about four micrometers by about four micrometers; from about two micrometers by about two micrometers; from about six micrometers by about six micrometers; or from about one micrometer by about one micrometer.

The example image sensor array **186** includes photodiodes that have a light-receiving surface and have substantially uniform length and width. During exposure, the photodiodes convert the incident light to a charge. The image sensor array **186** can be operated as a global reset, that is, substantially all of the photodiodes are exposed simultaneously and for substantially identical lengths of time.

The example fundus imaging system **102** also includes a display **108**, discussed in more detail above with reference to FIG. 1. Additionally, the example fundus imaging system **102** includes a computing device **1800**, discussed in more detail below with reference to FIG. 7.

FIG. 3 is an embodiment of a method **200** for imaging a patient's fundus using a fundus imaging system. In the embodiment shown, the lighting is optimally dimmed prior to execution, although lowering the lighting is optional. The embodiment shown includes a set depth of field operation **204**, a set number of zones operation **206**, an illuminate lighting operation **208**, an adjust lens focus operation **210**, a capture image operation **212**, repeat operation(s) **213**, a show images operation **214** and a determine representative image operation **216**. Other embodiments can include more or fewer steps.

The embodiment of method **200** begins with setting a depth of field operation **204**. In embodiments, the variable focus lens **180** is capable of focusing from about -20 diopters to about +20 diopters. Set depth of field operation **204** defines the lower and upper bounds in terms of diopters. For example, the depth of field range could be set to about -10 to +10 diopters; about -5 to about +5 diopters; about -10 to about +20 diopters; about -5 to about +20 diopters; about -20 to about +0 diopters; or about -5 to about +5 diopters. Other settings are possible. The depth of field can be preprogrammed by the manufacturer. Alternatively, the end user, such as the clinician C, can set the depth of field.

As shown in FIG. 3, the next operation in embodiment of method **200** is setting the number of zones operation **206**. However, zones operation **206** can occur before or concurrent with field operation **204**. In zones operation **206**, the depth of field is divided into equal parts, where each part is called a zone. In other embodiments, the zones are not all equal. The number of zones is equal to the number of images captured in capture image operation **212**.

For example, when the depth of field is from -10 to +10 diopters, the focus of the variable focus lens can be changed by 4 diopters before each image capture. Thus, in this example, images would be captured at -10, -6, -2, +2, +6 and +10 diopters. Or, images could be captured at -8, -4, 0, +4 and +8 diopters, thereby capturing an image in zones -10 to -6 diopters, -6 to -2 diopters, -2 to +2 diopters, +2 to +6 diopters and +6 to +10 diopters, respectively. In that instance, the depth of focus is about +/-2 diopters. Of course, the number of zones and the depth of field can vary, resulting in different ranges of depth of field image capture.

In embodiments, both depth of field and number of zones are predetermined. For example, -10D to +10D and 5 zones. Both can be changed by a user.

After the depth of field and number of zones are set, the next operation in embodiment of method **200** is the image capture process, which includes illuminate lighting operation **208**, adjust lens focus operation **210** and capture image operation **212**. As shown in FIG. 3, the lighting component is illuminated (lighting operation **208**) before the lens focus is adjusted (lens focus operation **210**). However, lens focus operation **210** can occur before or concurrent with lighting operation **208**.

The illumination LED **182** is illuminated in lighting operation **208**. The illumination LED **182** can remain illuminated throughout the duration of each image capture. Alternatively, the illumination LED **182** can be turned on and off for each image capture. In embodiments, the illumination LED **182** only turns on for the same period of time as the image sensor array **186** exposure time period.

Optionally, lighting operation **208** can additionally include illuminating a near-infrared LED. The clinician C can use the illumination of the near-infrared LED as a way to preview the position of the patient's P pupil.

The focus of variable focus lens **180** is adjusted in lens focus operation **210**. Autofocusing is not used in embodiment of method **200**. That is, the diopter setting is provided to the lens without regard to the quality of the focus of the image. Indeed, traditional autofocus fails in the low-lighting non-mydratic image capturing environment. The embodiment of method **200** results in a plurality of images at least one of which, or a combination of which, yields an in-focus view of the patient's P fundus.

Additionally, the lack of autofocus enables the fundus imaging system **102** to rapidly capture multiple images in capture image operation **212** at different diopter ranges. That is, variable focus lens **180** can be set to a particular diopter range and an image captured without the system verifying that the particular focus level will produce an in-focus image, as is found in autofocus systems. Because the system does not attempt to autofocus, and the focus of the variable focus lens **180** can be altered in roughly tens of milliseconds, images can be captured throughout the depth of field in well under a second, in embodiments. Thus, in the embodiment of method **200**, the fundus imaging system **102** can capture images of the entire depth of field before the patient's P eye can react to the illuminated light. Without being bound to a particular theory, depending on the patient P, the eye might react to the light from illumination LED **182** in about 150 milliseconds.

The image sensor array **186** captures an image of the fundus in capture image operation **212**. As discussed above, the embodiment of method **200** includes multiple image captures of the same fundus at different diopter foci. The example fundus imaging system **102** uses a global reset or global shutter array, although other types of shutter arrays, such as a rolling shutter, can be used. The entire image capture method **200** can also be triggered by passive eye tracking and automatically capture, for example, 5 frames of images. An embodiment of example method for passive eye tracking is shown and described in more detail with reference to FIG. 5, below.

After the fundus imaging system **102** captures an image of the fundus, the embodiment of method **200** returns in loop **213** to either the illuminate lighting operation **208** or the adjust lens focus operation **210**. That is, operations **208**, **210** and **212** are repeated until an image is captured in each of the preset zones from zones operation **206**. It is noted that the image capture does not need to be sequential through the depth of field. Additionally, each of the images does not need

to be captured in a single loop; a patient could have one or more fundus images captured and then one or more after a pause or break.

After an image is captured in each of the zones (capture image operation 212) in embodiment of method 200, either the images are displayed in show images operation 214 or a representative image is determined in operation 216 and then the image is displayed. Show images operation 214 can include showing all images simultaneously or sequentially on display 108. A user interface shown on display 108 can then enable the clinician C or other reviewing medical professional to select or identify the best or a representative image of the patient's P fundus.

In addition to, or in place of, show images operation 214, the computing device can determine a representative fundus image in operation 216. Operation 216 can also produce a single image by compiling aspects of one or more of the images captured. This can be accomplished by, for example, using a wavelet feature reconstruction method to select, interpolate, and/or synthesize the most representative frequency or location components.

The fundus imaging system 102 can also produce a three-dimensional image of the fundus by compiling the multiple captured images. Because the images are taken at different focus ranges of the fundus, the compilation of the pictures can contain three-dimensional information about the fundus.

In turn, the image or images from operation 214 or 216 can be sent to a patient's electronic medical record or to a different medical professional via network 110.

FIG. 4 illustrates an embodiment of example fundus imaging system 400. The embodiment 400 includes a housing 401 that supports an optional fixation LED 402, an objective lens 404, fixation LED mirrors 405, variable focus lens assembly 406, display 408, printed circuit board 410, step motor 412, image sensor array 414, and illumination LED 416. Also shown in FIG. 4 are light paths L that include potential light paths from optional fixation LED 402 and incoming light paths from outside the fundus imaging system 400. The illustrated components have the same or similar functionality to the corresponding components discussed above with reference to FIGS. 1-3 above. Other embodiments can include more or fewer components.

The housing 401 of example fundus imaging system 400 is sized to be hand held. In embodiments, the housing 401 additionally supports one or more user input buttons near display 408, not shown in FIG. 4. The user input button can initiate the image capture sequence, at least a portion of which is shown and discussed with reference to FIG. 3, above. Thus, the fundus imaging system 400 is capable of being configured such that the clinician C does not need to adjust the lens focus.

Fixation LED 402 is an optional component of the fundus imaging system 400. The fixation LED 402 is a single or multi-colored LED. Fixation LED 402 can be more than one LED.

As shown in FIG. 4, pivoting mirrors 405 can be used to direct light from the fixation LED 402 towards the patient's pupil. Additionally, an overlay or filter can be used to project a particular shape or image, such as an "X", to direct the patient's focus. The pivoting mirrors 405 can control where the fixation image appears in the patient's view. The pivoting mirrors 405 do not affect the light reflected from the patient's fundus.

The embodiment of example fundus imaging system 400 also includes a variable focus lens assembly 406. As shown in FIG. 4, the variable focus lens assembly 406 is substan-

tially aligned with the longitudinal axis of the housing 401. Additionally, the variable focus lens assembly 406 is positioned between the objective lens 404 and the image sensor array 414 such that it can control the focus of the incident light L onto the image sensor array.

The example printed circuit board 410 is shown positioned within one distal end of the housing 401 near the display 408. However, the printed circuit board 410 can be positioned in a different location. The printed circuit board 410 supports the components of the example computing device 1800. A power supply can also be positioned near printed circuit board 410 and configured to power the components of the embodiment of example fundus imaging system 400.

Step motor 412 is an optional component in the example embodiment 400. Step motor 412 can also be, for example, a voice coil, an ultrasonic motor, or a piezoelectric actuator. In the example embodiment 400, step motor 412 moves the variable focus lens assembly 406 and/or the sensor array 414 to achieve variable focus. The step motor 412 moves the variable focus lens assembly 406 or the sensor array 414 in a direction parallel to a longitudinal axis of the housing 401 (the optical axis). The movement of step motor 412 is actuated by computing device 1800.

The example image sensor array 414 is positioned normal to the longitudinal axis of the housing 401. As discussed above, the image sensor array 414 is in electrical communication with the computing device. Also, as discussed above, the image sensor array can be a CMOS (APS) or CCD sensor.

An illumination LED 416 is positioned near the variable focus lens assembly 406. However, the illumination LED 416 can be positioned in other locations, such as near or with the fixation LED 402.

FIG. 5 illustrates an alternate embodiment of initiate retinal imaging step 306 using passive eye tracking. The initiate retinal imaging step 306 operates to image the fundus of the patient P using passive eye tracking. In the initiate retinal imaging step 306, the fundus imaging system 102 monitors the pupil/fovea orientation of the patient P. Although the initiate retinal imaging step 306 is described with respect to fundus imaging system 102, the initiate retinal imaging step 306 may be performed using a wearable or nonwearable fundus imaging system, such as a handheld digital fundus imaging system.

Initially, at step 303, the pupil or fovea or both of the patient P are monitored. The fundus imaging system 102 captures images in a first image capture mode. In the first image capture mode, the fundus imaging system 102 captures images at a higher frame rate. In some embodiments, in the first image capture mode, the fundus imaging system 102 captures images with infra-red illumination and at lower resolutions. In some embodiments, the infra-red illumination is created by the illumination LED 182 operating to generate and direct light of a lower intensity towards the subject. The first image capture mode may minimize discomfort to the patient P, allow the patient P to relax, and allow for a larger pupil size without dilation (non-mydratic).

Next, at step 305, the computing system 1800 processes at least a portion of the images captured by the fundus imaging system 102. The computing system 1800 processes the images to identify the location of the pupil or fovea or both of the patient P. Using the location of the pupil or fovea or both in one of the images, a vector corresponding to the pupil/fovea orientation is calculated. In some embodiments, the pupil/fovea orientation is approximated based on the

distance between the pupil and fovea in the image. In other embodiments, the pupil/fovea orientation is calculated by approximating the position of the fovea relative to the pupil in three dimensions using estimates of the distance to the pupil and the distance between the pupil and the fovea. In other embodiments, the pupil/fovea orientation is approximated from the position of the pupil alone. In yet other embodiments, other methods of approximating the pupil/fovea orientation are used.

Next, at step 307, the pupil/fovea orientation is compared to the optical axis of the fundus imaging system 102. If the pupil/fovea orientation is substantially aligned with the optical axis of the fundus imaging system 102, the process proceeds to step 309 to capture a fundus image. If not, the process returns to step 303 to continue to monitor the pupil or fovea. In some embodiments, the pupil/fovea orientation is substantially aligned with the optical axis when the angle between them is less than two to fifteen degrees.

Next, at step 309, fundus images are captured by triggering the embodiment of example thru focusing image capturing method 200. In embodiments, five images are captured at step 309. In some embodiments, the fundus image is captured in a second image capture mode. In some embodiments, in the second image capture mode, the fundus imaging system 102 captures images with visible illumination and at higher resolutions. In some embodiments, the visible illumination is created by the illumination LED 182 operating to generate and direct light of a higher intensity towards the subject. In other embodiments, the higher illumination is created by an external light source or ambient light. The second image capture mode may facilitate capturing a clear, well-illuminated, and detailed fundus image.

In some embodiments, after step 309, the initiate retinal imaging step 306 returns to step 303 to continue to monitor the pupil/fovea orientation. The initiate retinal imaging step 306 may continue to collect fundus images indefinitely or until a specified number of images have been collected. Further information regarding passive eye tracking can be found in U.S. patent application Ser. No. 14/177,594, titled Ophthalmoscope Device, which is hereby incorporated by reference in its entirety.

FIG. 6 is an embodiment of example use 500 of fundus imaging system 102. In the embodiment of example use 500, a clinician positions the fundus imaging system (operation 502), initiates image capture (operation 504), positions the fundus imaging system over the other eye (operation 506), initiates image capture (operation 508), and views images (operation 520). Although the example use 500 is conducted without first administering mydriatic pharmaceuticals, the example use 500 can also be performed for a patient who has taken a pupil-dilating compound. The embodiment of example use 500 can also include lowering the lighting. The embodiment of example use 500 is conducted using the same or similar components as those described above with reference to FIGS. 1-3. Other embodiments can include more or fewer operations.

The embodiment of example use 500 begins by positioning the fundus imaging system (operation 502). In embodiments, the clinician first initiates an image capture sequence via a button on the housing or a graphical user interface shown by the display. The graphical user interface can instruct the clinician to position the fundus imaging system over a particular eye of the patient. Alternatively, the clinician can use the graphical user interface to indicate which eye fundus is being imaged first.

In operation 502, the clinician positions the fundus imaging system near the patient's eye socket. The clinician

positions the aperture of the system flush against the patient's eye socket such that the aperture, or a soft material eye cup extending from the aperture, seals out most of the ambient light. Of course, the example use 500 does not require positioning the aperture flush against the patient's eye socket.

When the fundus imaging system is in position, the system captures more than one image of the fundus in operation 504. As discussed above, the system does not require the clinician to manually focus the lens. Additionally, the system does not attempt to autofocus on the fundus. Rather, the clinician simply initiates the image capture, via a button or the GUI, and the fundus imaging system controls when to capture the images and the focus of the variable focus lens. Also, as discussed above at least with reference to FIG. 5, the system can initiate image capture using passive eye tracking.

The patient may require the fundus imaging system to be moved away from the eye socket during image capture operation 504. The clinician can re-initiate the image capture sequence of the same eye using the button or the GUI on the display.

After capturing an image in each of the specified zones, the fundus imaging system notifies the clinician that the housing should be positioned over the other eye (operation 506). The notification can be audible, such as a beep, and/or the display can show a notification. In embodiments, the system is configured to capture a set of images of only one eye, wherein the example method 500 proceeds to view images operation 520 after image capture operation 504.

Similar to operation 502, the clinician then positions the fundus imaging system near or flush with the patient's other eye socket in operation 506. Again, when the system is in place, an image is captured in every zone in operation 508.

After images have been captured of the fundus in each pre-set zone, the clinician can view the resulting images in operation 520. As noted above with reference to FIG. 3, the images can be post-processed before the clinician views the images to select or synthesize a representative image. Additionally, the fundus images can be sent to a remote location for viewing by a different medical professional.

FIG. 7 is a block diagram illustrating physical components (i.e., hardware) of a computing device 1800 with which embodiments of the disclosure may be practiced. The computing device components described below may be suitable to act as the computing devices described above, such as wireless computing device and/or medical device of FIG. 1. In a basic configuration, the computing device 1800 may include at least one processing unit 1802 and a system memory 1804. Depending on the configuration and type of computing device, the system memory 1804 may comprise, but is not limited to, volatile storage (e.g., random access memory), non-volatile storage (e.g., read-only memory), flash memory, or any combination of such memories. The system memory 1804 may include an operating system 1805 and one or more program modules 1806 suitable for running software applications 1820. The operating system 1805, for example, may be suitable for controlling the operation of the computing device 1800. Furthermore, embodiments of the disclosure may be practiced in conjunction with a graphics library, other operating systems, or any other application program and is not limited to any particular application or system. This basic configuration is illustrated in FIG. 7 by those components within a dashed line 1808. The computing device 1800 may have additional features or functionality. For example, the computing device 1800 may also include additional data storage devices (removable and/or non-

removable) such as, for example, magnetic disks, optical disks, or tape. Such additional storage is illustrated in FIG. 7 by a removable storage device **1809** and a non-removable storage device **1810**.

As stated above, a number of program modules and data files may be stored in the system memory **1804**. While executing on the processing unit **1802**, the program modules **1806** may perform processes including, but not limited to, generate list of devices, broadcast user-friendly name, broadcast transmitter power, determine proximity of wireless computing device, connect with wireless computing device, transfer vital sign data to a patient's EMR, sort list of wireless computing devices within range, and other processes described with reference to the figures as described herein. Other program modules that may be used in accordance with embodiments of the present disclosure, and in particular to generate screen content, may include electronic mail and contacts applications, word processing applications, spreadsheet applications, database applications, slide presentation applications, drawing or computer-aided application programs, etc.

Furthermore, embodiments of the disclosure may be practiced in an electrical circuit comprising discrete electronic elements, packaged or integrated electronic chips containing logic gates, a circuit utilizing a microprocessor, or on a single chip containing electronic elements or microprocessors. For example, embodiments of the disclosure may be practiced via a system-on-a-chip (SOC) where each or many of the components illustrated in FIG. 7 may be integrated onto a single integrated circuit. Such an SOC device may include one or more processing units, graphics units, communications units, system virtualization units and various application functionality all of which are integrated (or "burned") onto the chip substrate as a single integrated circuit. When operating via an SOC, the functionality, described herein, may be operated via application-specific logic integrated with other components of the computing device **1800** on the single integrated circuit (chip). Embodiments of the disclosure may also be practiced using other technologies capable of performing logical operations such as, for example, AND, OR, and NOT, including but not limited to mechanical, optical, fluidic, and quantum technologies. In addition, embodiments of the disclosure may be practiced within a general purpose computer or in any other circuits or systems.

The computing device **1800** may also have one or more input device(s) **1812** such as a keyboard, a mouse, a pen, a sound or voice input device, a touch or swipe input device, etc. The output device(s) **1814** such as a display, speakers, a printer, etc. may also be included. The aforementioned devices are examples and others may be used. The computing device **1800** may include one or more communication connections **1816** allowing communications with other computing devices. Examples of suitable communication connections **1816** include, but are not limited to, RF transmitter, receiver, and/or transceiver circuitry; universal serial bus (USB), parallel, and/or serial ports.

The term computer readable media as used herein may include non-transitory computer storage media. Computer storage media may include volatile and nonvolatile, removable and non-removable media implemented in any method or technology for storage of information, such as computer readable instructions, data structures, or program modules. The system memory **1804**, the removable storage device **1809**, and the non-removable storage device **1810** are all computer storage media examples (i.e., memory storage.) Computer storage media may include RAM, ROM, electri-

cally erasable read-only memory (EEPROM), flash memory or other memory technology, CD-ROM, digital versatile disks (DVD) or other optical storage, magnetic cassettes, magnetic tape, magnetic disk storage or other magnetic storage devices, or any other article of manufacture which can be used to store information and which can be accessed by the computing device **1800**. Any such computer storage media may be part of the computing device **1800**. Computer storage media does not include a carrier wave or other propagated or modulated data signal.

Communication media may be embodied by computer readable instructions, data structures, program modules, or other data in a modulated data signal, such as a carrier wave or other transport mechanism, and includes any information delivery media. The term "modulated data signal" may describe a signal that has one or more characteristics set or changed in such a manner as to encode information in the signal. By way of example, and not limitation, communication media may include wired media such as a wired network or direct-wired connection, and wireless media such as acoustic, radio frequency (RF), infrared, and other wireless media.

Although the example medical devices described herein are devices used to monitor patients, other types of medical devices can also be used. For example, the different components of the CONNEX™ system, such as the intermediary servers that communication with the monitoring devices, can also require maintenance in the form of firmware and software updates. These intermediary servers can be managed by the systems and methods described herein to update the maintenance requirements of the servers.

FIG. 8 shows another embodiment of logical components of the fundus imaging system **102**. In this example, the fundus imaging system **102** includes image capture module **602**, 3-dimensional map module **604**, and screening module **606**. Other embodiments can include more or fewer modules.

The fundus imaging system **102** is programmed to execute the modules **602**, **604**, **606** according to firmware and/or software accessible to the fundus imaging system **102**. For example, a processing unit of the fundus imaging system **102** executes software stored on computer readable media to implement the modules **602**, **604**, **606**.

Image capture module **602** receives image capture requests and coordinates capturing of a plurality of images. For instance, image capture module **602** receives a screening request and coordinates image capture by camera **104** at various focal lengths. In some embodiments, image capture module **602** also coordinates illumination of a visible light component during or before image capture.

Typically, image capture module **602** defines a depth of field or receives a depth of field from a user. In some instances, the depth of field is from -6 diopters to $+6$ diopters. Another example depth of field is from -10 diopters to $+10$ diopters. Other depths of field are contemplated.

Image capture module **602** also determines, or receives instructions, the incremental focus changes within the depth of field. As an example, the focus is altered by ± 3 diopters between each image capture. Other incremental focus changes, such as ± 1 diopter, ± 2 diopters, etc., are contemplated. Of note is that the image capture module **602** does not use autofocus during image capture. Thus, various aspects of the imaged fundus may be in focus or out of focus in the captured images.

Within the depth of field, image capture module **602** instructs camera **104** to capture an image at a starting focus,

at each incremental focus within the depth of field, and at an ending focus. For example, in a depth of field of -6 diopters to $+6$ diopters, and with an incremental focus change of ± 3 diopters, image capture module **602** causes camera **104** to capture an image at -6 diopters, -3 diopters, 0 diopters, 3 diopters, and 6 diopters. As described above, all of the images are captured in a period of time that is typically less than about 150 milliseconds.

Three-dimensional map module **604** receives the captured images and generates a three-dimensional map of the fundus. Generally, three-dimensional maps are generated by comparing specific pixels and/or regions across the corresponding pixels and/or regions of all the captured images. Based on which attributes are in focus or out of focus in the captured images, relative peaks and valleys can be determined and a topography of the fundus generated.

In some embodiments, three-dimensional maps are generated by defining a first region and grading a focus quality of that region for each of the captured images. The first region may include one or more pixels. An example region is a 5 pixel by 5 pixel region, where one corner starts at coordinates $(0,0)$ and a diagonal corner is located at $(4, 4)$. Each image captured in the sequence has a 5 pixel by 5 pixel region at those coordinates.

Each region is evaluated for focus quality on a scale, such as 0-100. Focus quality may be determined using a local focus metric such as sum of modified Laplacian (SML). Based on the change of the focus quality of that region across the images a slope of the imaged surface can be determined. Additionally, or alternatively, the images where the region is most in focus can be used to determine peaks and/or valleys. As an example, a pixel at (i, j) has a de-focused image (by SML) at -6 diopters, so the pixel (i, j) corresponds to a best focus in the 0 diopter image, which is the lowest valley point. Accordingly, -3 diopters corresponds to a median valley point, $+3$ diopters corresponds to a median ridge point, and $+6$ diopters corresponds to the highest ridge point.

Neighboring regions, and the slopes determined thereof, can be used to cross-check the determined slope for a given region. The process is repeated for all regions in each corresponding image. Then, the slopes of all the regions can be used to generate a three-dimensional map of the fundus.

Screening module **606** analyzes the three-dimensional map of the fundus generated by three-dimensional map module **604**. Screening module **606** can be used to screen for various conditions or diseases. Additionally, screening module **606** can be used to diagnose various conditions or diseases. For example, screening module **606** may screen or diagnose macular edema (by detecting unusual swelling in foveal area), papilledema (by detecting unusual swelling in an optic nerve), epi-retinal membrane (by detecting translucent membrane structure on top of foveal/macular area), and/or glaucoma (by detecting unusual cup-to-disc ratio three-dimensionally). Screening module **606** may also determine a disease stage, such as the stage of papilledema and/or optic nerve edema.

In some embodiments, screening module **606** screens for, or diagnoses, based on analyzing one or more areas of interest on the three-dimensional map. For instance, screening module **606** may start the analysis by identifying irregularities in the fundus surface, such as peaks and/or valleys. In some instances, peaks may correspond to swelling and the swelling may be related to one or more diseases.

Screening module **606** may use one or more thresholds in the disease screening and/or diagnosis. For example, any peak in foveal area greater than 100 microns is flagged for

physician review. As another example, any swelling in foveal area greater than 300 microns is diagnosed as indicative of macular edema. In some instances, screening module **606** causes a display to show an image or text representative of the screening and/or diagnosis result.

FIG. 9 is an example method **700** of processing a set of fundus images captured by fundus imaging system **102**. The example method **700** includes determining a pixel location (operation **702**), calculating a focus quality score (operation **704**), determining a best focus quality score plane (operation **706**), and scaling using a best focus quality score plane (operation **708**). Example method **700** is typically repeated for other pixel locations. Other embodiments can include more or fewer operations.

FIGS. 10A-10E, discussed in conjunction with FIG. 9 below, are an example set of fundus images **800**, **810**, **820**, **830**, **840** captured by an embodiment of fundus imaging system **102**. The example fundus images **800**, **810**, **820**, **830**, **840** were captured with a focus at -2 diopters, -1 diopter, 0 diopter, $+1$ diopter, and $+2$ diopters, respectively.

Example method **700** begins by determining a pixel location (operation **702**) for analysis. The pixel location may be identified by coordinates, such as (i, j) . For each image in the set, the same pixel location is analyzed. An example pixel location **802**, **812**, **822**, **832**, **842** for each image **800**, **810**, **820**, **830**, **840**, respectively, is shown in FIGS. 10A-10E. The pixel location **802**, **812**, **822**, **832**, **842** shown in FIGS. 10A-10E includes a pixel and a neighborhood window. In FIGS. 10A-10E, a neighborhood window of 5 pixels by 5 pixels is used, however, other neighborhood window sizes are contemplated.

After the pixel location is determined (operation **702**), a focus quality score is calculated (operation **704**). A focus quality score is calculated (operation **704**) for each pixel location **802**, **812**, **822**, **832**, **842**, usually including the neighborhood window. In some embodiments, a focus quality score is determined using sum of modified Laplacian (SML). In some embodiments, a focus quality score is determined using variance of Laplacian (VOL). Methods and techniques for calculating a focus quality score are described in more detail above with reference, at least, to FIG. 8. Various scoring scales may be used, such as a numerical scale, for example, a range of 0.0-1.0 or 0-100.

After calculating a focus quality score (operation **704**), a best focus quality score plane is determined (operation **706**). In some embodiments, determining a best focus quality score (operation **706**) includes determining which image in the set of images has the highest focus quality score at the identified pixel location. In effect, determining the image with the best focus quality also determines the plane (perpendicular to the focal axis) that is best in focus at the pixel location. In some instances, operation **706** can include determining a location between frames (images) where the best focus is likely present. For example, operation **706** may determine that between the image captured at $+1$ diopter and $+2$ diopters lies the best focus.

After determining a best focus quality score (operation **706**), the images are scaled (operation **708**). Scaling the images using the best focus quality score includes determining a multiplier, where the multiplier may be based on the image resolution. In the example shown in FIGS. 10A-10E, the images are scaled by a multiplier of 370 microns per diopter. The scaled values are then used when generating the three-dimensional image.

After scaling the images (operation **708**), a determination is made whether additional pixel locations need to be analyzed (operation **710**). If the determination is that more

pixel locations need to be analyzed, example method 700 returns to determine a pixel location (operation 702) that has not yet been analyzed. If the determination is that no more pixel locations need to be analyzed, then example method 700 proceeds to generate a three-dimensional image (operation 712).

Generating a three-dimensional image (operation 712) includes using the best focus images and scaling determined in operations 706 and 708. As an example, at pixel location P1, the best focus score was at the image captured at -2 diopters, at pixel location P2, the best focus score was at the image captured at 0 diopters, and at pixel location P3, the best focus score was at the image captured at -1 diopter. Then, using the scaling of operation 708, the three-dimensional map of P1, P2, P3 will be at -740 microns, 0 micron, and -370 microns.

Embodiments of the present invention may be utilized in various distributed computing environments where tasks are performed by remote processing devices that are linked through a communications network in a distributed computing environment.

The block diagrams depicted herein are just examples. There may be many variations to these diagrams described therein without departing from the spirit of the disclosure. For instance, components may be added, deleted or modified.

While embodiments have been described, it will be understood that those skilled in the art, both now and in the future, may make various improvements and enhancements can be made.

As used herein, "about" refers to a degree of deviation based on experimental error typical for the particular property identified. The latitude provided the term "about" will depend on the specific context and particular property and can be readily discerned by those skilled in the art. The term "about" is not intended to either expand or limit the degree of equivalents which may otherwise be afforded a particular value. Further, unless otherwise stated, the term "about" shall expressly include "exactly," consistent with the discussions regarding ranges and numerical data. Concentrations, amounts, and other numerical data may be expressed or presented herein in a range format. It is to be understood that such a range format is used merely for convenience and brevity and thus should be interpreted flexibly to include not only the numerical values explicitly recited as the limits of the range, but also to include all the individual numerical values or sub-ranges encompassed within that range as if each numerical value and sub-range is explicitly recited. As an illustration, a numerical range of "about 4 percent to about 7 percent" should be interpreted to include not only the explicitly recited values of about 4 percent to about 7 percent, but also include individual values and sub-ranges within the indicated range. Thus, included in this numerical range are individual values such as 4.5, 5.25 and 6 and sub-ranges such as from 4-5, from 5-7, and from 5.5-6.5; etc. This same principle applies to ranges reciting only one numerical value. Furthermore, such an interpretation should apply regardless of the breadth of the range or the characteristics being described.

The description and illustration of one or more embodiments provided in this application are not intended to limit or restrict the scope of the invention as claimed in any way. The embodiments, examples, and details provided in this application are considered sufficient to convey possession and enable others to make and use the best mode of claimed invention. The claimed invention should not be construed as being limited to any embodiment, example, or detail pro-

vided in this application. Regardless whether shown and described in combination or separately, the various features (both structural and methodological) are intended to be selectively included or omitted to produce an embodiment with a particular set of features. Having been provided with the description and illustration of the present application, one skilled in the art may envision variations, modifications, and alternate embodiments falling within the spirit of the broader aspects of the claimed invention and the general inventive concept embodied in this application that do not depart from the broader scope.

What is claimed is:

1. A non-mydratic fundus imaging apparatus, the apparatus comprising:

a processor and memory; and

a camera including a lens, the camera operatively coupled to the processor,

wherein the memory stores instructions that, when executed by the processor, cause the apparatus to:

adjust a focus of the lens to a plurality of different diopter ranges;

capture a plurality of images of a fundus, wherein the camera captures at least one image at each of the plurality of different diopter ranges; and

after capturing each of the plurality of images of the fundus, generate a three-dimensional map of the fundus using each of the plurality of images of the fundus, including:

identify a first region, each of the plurality of images having corresponding first regions;

evaluate each of the respective first regions of each of the plurality of images for focus quality, thereby generating a focus quality score for each of the respective first regions of each of the plurality of images;

generate a slope of the fundus based on a change in the focus quality score in the first regions across the plurality of images of the fundus; and

use the slope to generate the three-dimensional map of the fundus.

2. The apparatus according to claim 1, the instructions further causing the apparatus to:

identify one or more areas of interest on the three-dimensional map of the fundus; and

screen the one or more areas of interest for indications of disease.

3. The apparatus according to claim 1, the instructions further causing the apparatus to:

identify one or more areas of interest on the three-dimensional map of the fundus; and

identify a diagnosis based on the one or more areas of interest.

4. The apparatus of claim 3, the diagnosis including a determination of whether the three dimensional map is indicative of papilledema.

5. The apparatus according to claim 4, the diagnosis further including a determination of a stage of papilledema.

6. The apparatus according to claim 3, further comprising a display coupled to the memory and to the processor and configured to display an image or text representative of the diagnosis.

7. The apparatus according to claim 1, the instructions further causing the apparatus to:

adjust the focus of the lens and capture subsequent images until images have been captured of a depth of field from -6 diopters to +6 diopters.

8. The apparatus according to claim 6, wherein each adjustment of the focus is by ± 3 diopters.

9. The apparatus according to claim 1, wherein the images are captured sequentially in less than about 150 milliseconds.

10. The apparatus according to claim 1, further comprising a visible light component configured to illuminate during the capture of the plurality of images.

11. A method for screening for optic nerve edema with a non-mydratic fundus imaging apparatus, the method comprising:

adjusting a lens of a camera to focus on each of a plurality of different diopter ranges in a depth of field;

capturing at least one image at each of the plurality of different diopter ranges;

generating a three-dimensional map of a fundus using the at least one image captured at each of the plurality of different diopter ranges, including:

identifying a first region, each of the images having corresponding first regions;

evaluating each of the respective first regions of each of the images for focus quality, thereby generating a focus quality score for each of the respective first regions of each of the plurality of images;

generating a slope of the fundus based on a change in the focus quality score in the first regions across the plurality of images of the fundus; and

using the slope to generate the three-dimensional map of the fundus; and

based on the three-dimensional map, screening for optic nerve edema.

12. The method according to claim 11, further comprising identifying one or more areas of interest on the three-dimensional map of the fundus, wherein the screening for optic nerve edema includes analyzing the one or more areas of interest.

13. The method according to claim 12, wherein screening for optic nerve edema includes identifying a diagnosis.

14. The method according to claim 13, further comprising displaying an indication of the diagnosis on a display.

15. The method according to claim 12, wherein the depth of field is from -6 diopters to 6 diopters.

16. A non-mydratic fundus image capture system, comprising:

a housing;

an image capture device coupled to the housing, the image capture device including a visible light component configured to illuminate;

a display;

a processing unit; and

memory storing instructions that, when executed by the processing unit, cause the system to:

capture a plurality of images of a fundus in an image capture mode,

wherein the image capture mode includes a plurality of adjustments of a lens of the image capture device such that the image capture device captures an image at each of the plurality of adjustments in a depth of field focus range, wherein the light from the visible light component is gathered in a single step for each image;

after capturing each of the plurality of images of the fundus, generate a three-dimensional map of the fundus using each of the plurality of images of the fundus, including:

identify a first region, each of the plurality of images having corresponding first regions;

evaluate each of the respective first regions of each of the plurality of images for focus quality, thereby generating a focus quality score for each of the respective first regions of each of the plurality of images;

generate a slope of the fundus based on a change in the focus quality score in the first regions across the plurality of images of the fundus; and

use the slope to generate the three-dimensional map of the fundus;

identify one or more areas of interest on the three-dimensional map of the fundus; and

screen the one or more areas of interest for indications of disease.

17. The non-mydratic fundus image capture system according to claim 16, the instructions further causing the apparatus to:

identify a diagnosis based on the one or more areas of interest; and

display a diagnosis image representing the diagnosis.

18. The non-mydratic fundus image capture system according to claim 17, the instructions further causing the apparatus to adjust the focus of the lens and capture subsequent images until images have been captured of a depth of field from -6 diopters to $+6$ diopters, wherein each adjustment of the focus is by ± 3 diopters.

19. The apparatus according to claim 1, wherein the first region is a 5 pixel by 5 pixel region.

20. The apparatus according to claim 19, wherein slopes are generated for regions neighboring the first region.

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